REMARKS

Status of the Claims

Claims 16 and 19 are currently pending.

Claim Amendment

As a general comment, claim 16 has been amended to remove the reference to "valproate compound". This phrase has been replaced with the phrase "divalproex sodium". Additionally, claim 16 has been amended to recite "an oral" hydrophilic matrix formulation . Claim 19 has been deleted. No new matter has been added as a result of these amendments.

Claim Rejections – 35 U.S.C. Section 112

Claims 16 and 19 are rejected under 35 U.S.C. Section 112, first paragraph, as not being enabling. Specifically, the Examiner argues that the specification is enabling for very specific oral formulations having specific ingredients to deliver divalproex sodium but is not enabling for any pharmaceutical formulation comprising any valproate compounds. Applicants respectfully traverse.

While not agreeing with the Examiner, in order to expedite prosecution, claim 16 has been amended to recite divalproex sodium. Additionally, claim 16 have been amended to recite that the formulation is an "oral" formulation. Dependent claim 19 has been deleted. Therefore, in view of this amendment, this rejection is now moot and should be withdrawn.

Double Patenting

Claims 16 and 19 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over: (1) claims 1-16 of U.S. Patent No. 6,419,953; (2) claims 1-8 of U.S. Patent No. 6,511,678; (3) claims 1-7 of U.S. Patent No. 6,528,090; (4) 1-2 of U.S. Patent No. 6,528,091; (5) claims 1-3 of U.S. Patent No. 6,720,004; (6) 1-17 of U.S. Patent No. 6,713,086; and (7) claims 46-59 of copending Application No. 10/770,290.

Applicants wish to hold this rejection in abeyance until notification from the Examiner of allowable subject matter. Upon receipt from the Examiner of allowable subject matter, Applicants will file the appropriate terminal disclaimers to obviate the above rejections.

Claim Rejections – 35 U.S.C. Section 102(b)

Claims 16 and 19 are rejected under 35 U.S.C. Section 102(b) as anticipated by "Epilimchrono: A Multidose, Crossover Comparison of Two Formulations of Valproate in Healthy Volunteers", by Roberts et al. According to the Examiner, Roberts et al. disclose a once a day controlled release formulation to deliver divalproex sodium. The Examiner says that the Epilim Chrono formulation disclosed by Roberts et al. comprises valproate compounds and the hydrophilic polymer "ethylcellulose" as evidenced by the patient information leaflet of the product. The Examiner argues that Epilim Chrono is also in the form of a matrix formulation as defined by Applicants on page 12. Moreover, the Examiner says that Roberts et al. provide a comparison between a once a day formulation and a twice a day formulation and that this comparison shows that the once a day formulation of 1000 mg was almost identical to the enteric coated twice a day formulation. Applicants respectfully traverse.

As noted previously herein, claim 19 has been deleted. Moreover, claim 16 has been amended to recite divalproex sodium and that the formulation is an "oral" formulation.

Roberts et al. disclose the results of an investigation that compared the steady state pharmacokinetics and relative bioequivalence of a mixture of sodium valproate and valproic acid administered twice daily (500 mg Epilim® Chrono b.d.) or once daily (1000 mg Epilim® Chrono o.d.) and an enteric coated tablet containing only sodium valproate administered twice daily (500 mg Epilim® EC b.d) (See page 176). The study concluded that the once-daily Chrono regimen was bioequivalent to the twice-daily EC and Chrono formulations with respect to AUC, that the half-life was more or less identical and that the Cmin and Cmax at steady state for the once-daily Chrono were almost identical to those for the twice-daily EC regimen.

Roberts et al. simply do not disclose an oral hydrophilic matrix formulation that contains sodium valproate that can be administered once per day. The sodium valproate composition described by Roberts et al. is administered twice daily. In addition, there is absolutely nothing in Roberts et al. that discloses or suggest the claimed *in-vitro* dissolution profile. The Examiner argues that the claimed *in-vitro* dissolution profile is inherent. Applicants submit that the Examiner has not met her burden of establishing that the Roberts et al. formulations would have inherently the same

dissolution profile as the claimed formulation. Specifically, in order to establish inherency, the extrinsic evidence must establish and make clear that the missing descriptive matter would necessarily be present in the thing described in the prior art and that it would have been so recognized by one skilled in the art (See, *MPEP* Section 2112). It is also well known that inherency cannot be established by probabilities or possibilities. *Id.* Just because a certain thing may result from a given set of circumstances is not sufficient. *Id.* Moreover, with respect to the burden of proof in connection with an inherency rejection, the *MPEP* Section 2112 states that:

> In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original) (Applicant's invention was directed to a biaxially oriented, flexible dilation catheter balloon (a tube which expands upon inflation) used, for example, in clearing the blood vessels of heart patients). The examiner applied a U.S. patent to Schjeldahl which disclosed injection molding a tubular preform and then injecting air into the preform to expand it against a mold (blow molding). The reference did not directly state that the end product balloon was biaxially oriented. It did disclose that the balloon was "formed from a thin flexible inelastic, high tensile strength, biaxially oriented synthetic plastic material." *Id.* at 1462 (emphasis in original). The examiner argued that Schjeldahl's balloon was inherently biaxially oriented. The Board reversed on the basis that the examiner did not provide objective evidence or cogent technical reasoning to support the conclusion of inherency.) (Emphasis original).

The Examiner has failed to provide any extrinsic evidence to establish that the formulations of Roberts et al. would necessarily have the same dissolution profile as the claimed formulation. Therefore, because each and every element of the claimed invention is not disclosed by Roberts et al., this rejection is improper and should be withdrawn.

Claims 16 and 19 are rejected under 35 U.S.C. Section 102(b) as being unpatentable over U.S. Patent No. 4,913,906. According to the Examiner, the '906 patent teaches a composition for the controlled release of salts of valproic acid comprising 10-80% of the active agent. The Examiner also says that the controlled release formulation results in sustained action fo the drug with small fluctuation of the plasma level over prolonged period of time (col. 1, lines 59-62). Moreover, the Examiner says that the composition is a once a day oral formulation that delivers the drug for 24 hours and shows about a 97% dissolution rate profile after 24 hours. Also, divalproex sodium is disclosed as one of the salts of valproic acid that is suitable for the formulation of the reference. Finally, the Examiner says that the "in dissolution profile is inherent for the formulation". Applicants respectfully traverse.

As noted previously herein, claim 19 has been deleted. Moreover, claim 16 has been amended to recite divalproex sodium and that the formulation is an "oral" formulation. While the '906 patent mentions divalproex sodium, all of the data provided in the examples is directed to compositions containing sodium valproate and valpromide. No *in vitro* dissolution data for divalproex sodium are provided. As with Roberts et al., the Examiner has failed to provide any **extrinsic evidence** to establish that the formulations of the '906 patent would necessarily have the same dissolution profile as the claimed formulation. Therefore, because each and every element of the claimed invention is not disclosed by the '906 patent, this rejection is improper and should be withdrawn.

REQUEST FOR RECONSIDERATION

Reconsideration and withdrawal of all claim rejections are respectfully requested. Applicants believe that the present application is in condition for allowance. Should the Examiner have any questions or would like to discuss any matters in connection with the present application, the Examiner is invited to contact the undersigned. If any additional fees are incurred as a result of the filing of this paper, authorization is given to charge deposit account number 04-2223.

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